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Nd:YAG laser vitreolysis versus pars plana vitrectomy for vitreous floaters (Review)

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TABLE OF CONTENTS

[Intervention Review]

Nd:YAG laser vitreolysis versus pars plana vitrectomy for vitreous floaters

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ABSTRACT

Background

The vitreous is the clear jelly of the eye and contains fine strands of proteins. Throughout life the composition of this vitreous changes, which causes the protein strands in it to bundle together and scatter light before it reaches the retina. Individuals perceive the shadows cast by these protein bundles as 'floaters'. Some people are so bothered by floaters that treatment is required to control their symptoms. Two major interventions for floaters include Nd:YAG laser vitreolysis and vitrectomy. Nd:YAG laser vitreolysis involves using laser energy to fragment the vitreous opacities via a non-invasive approach. Vitrectomy involves the surgical replacement of the patient's vitreous (including the symptomatic vitreous floaters) with an inert and translucent balanced salt solution, through small openings in the pars plana.

Objectives

To compare the effectiveness and safety of Nd:YAG laser vitreolysis to pars plana vitrectomy for symptomatic vitreous floaters.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 12), MEDLINE Ovid (1946 to 17 January 2017), Embase Ovid (1947 to 17 January 2017), LILACS (Latin American and Caribbean Health Sciences Literature Database) (1982 to 17 January 2017), the ISRCTN registry (www.isrctn.com/editAdvancedSearch); searched 17 January 2017, ClinicalTrials.gov (www.clinicaltrials.gov); searched 17 January 2017 and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en); searched 17 January 2017. We did not use any date or language restrictions in the electronic searches for trials. We also searched conference proceedings to identify additional studies.

Selection criteria

We included only randomised controlled trials (RCTs) that compared Nd:YAG laser vitreolysis to pars plana vitrectomy for treatment of symptomatic floaters.

Data collection and analysis

We planned to use methods recommended by Cochrane. The primary outcome we planned to measure was change in vision-related quality of life from baseline to 12 months, as determined by a vision-related quality of life questionnaire. The secondary outcomes we planned to measure were best corrected logMAR or Snellen visual acuity at 12 months for the treated eye(s) and costs. Adverse outcomes we planned

to record were the occurrence of sight-threatening complications by 12 months (asymptomatic retinal tears, symptomatic retinal tears, retinal detachment, cataract formation, and endophthalmitis).

Main results

No studies met the inclusion criteria of this review.

Authors' conclusions

There are currently no RCTs that compare Nd:YAG laser vitreolysis with pars plana vitrectomy for the treatment of symptomatic floaters. Properly designed RCTs are needed to evaluate the treatment outcomes from the interventions described. We recommend future studies randomise participants to either a Nd:YAG laser vitreolysis group or a vitrectomy group, with participants in each group assigned to either receive treatment or a sham intervention. Future studies should follow participants at six months and 12 months after the intervention. Also they should use best corrected visual acuity (BCVA) using an Early Treatment of Diabetic Retinopathy Study (ETDRS) chart read at 4 metres, vision-related quality of life (VRQOL), and adverse outcomes as the outcome measures of the trial.

PLAIN LANGUAGE SUMMARY

Laser or vitrectomy for vitreous floaters

What was the aim of this review?
The aim of this Cochrane Review was to find out whether laser or vitrectomy is the most effective and safe treatment for vitreous floaters.

Key messages
It is unclear whether or not laser or vitrectomy is better for the treatment of vitreous floaters.

What was studied in this review?

The eyeball is filled with a clear jelly-like material called vitreous. Sometimes strands of protein clump together in the vitreous. This can give the appearance of small shapes floating in the eye. This is a natural part of ageing, it is harmless, and usually does not need treatment. Larger floaters may be distracting and may make activities, such as reading and driving, difficult.

If floaters are causing vision problems, they can either be treated with laser or vitrectomy. Laser treatment is directed at the floater, which is then vaporised. Vitrectomy is a surgical treatment that involves complete removal of the vitreous.

What are the main results of the review?
The Cochrane researchers did not find any studies that directly compared these two types of treatments.

How up to date is this review?
The Cochrane researchers searched for studies published up to 17 January 2017.

BACKGROUND

Description of the condition

The vitreous is a translucent extracellular matrix that fills the region of the eye between the retina and lens. It is approximately 4.0 mL in volume, consists of over 98% water, and is gel-like in character. Its structural integrity is maintained by a dilute network of collagen fibrils interspersed with long arrays of hyaluronan molecules. The vitreous is responsible for maintaining the transparency of the eye and the uniform transmission of photons towards the retina for photoreception (Bishop 2000; Sebag 2009; Yanoff 2008). In the simplest sense, the vitreous separates into a liquid and solid component over time. When a pocket of liquid forms at the junction of the vitreous and retina the liquid may act as a wedge, forcing the vitreous and retina apart, until the vitreous peels off the retina completely before shrinking and relocating to behind the lens, where it can obstruct the normal transmission of light to the retina. This process is called posterior vitreous detachment.

In youth, the vitreous is clear with a homogeneous distribution of collagen and hyaluronan. As the vitreous ages, the collagen aggregates into tight parallel bundles bound by cross-links. This leaves pockets of liquid within the vitreous which have a paucity of these structural macromolecules. This molecular rearrangement is termed vitreous liquefaction, or syneresis (Sebag 2011). These liquefied pockets become more confluent towards the centre of the vitreous body. Over time, the liquid enters the potential space between the vitreous and retina, causing vitreoretinal dehiscence. This leads to the progressive collapse of the posterior vitreous away from the retina until ‘posterior vitreous detachment’ eventually occurs (Sebag 2009; Sebag 2011; Yanoff 2008).

These aggregated collagen bundles scatter incident photons. Patients may perceive a 'grey, silhouette-like, or spider web-like' artefact that has a short period of persistent momentum after cessation of eye movement. These visual artefacts are clinically termed 'floaters'. Floaters are caused by scattering of incident light at a localised region within the vitreous which casts a small shadow on the retina. Floaters can be particularly bothersome for patients if they reside close to the centre of the visual axis. The perception of floaters can also be caused by blood within the vitreous and glial cells torn from the optic disc (Sebag 2011; Sendrowski 2010).

Description of the intervention

Two major interventions for symptomatic floaters include neodymium-doped yttrium aluminium garnet (Nd:YAG) laser vitreolysis and vitrectomy.

Laser energy can be used to fragment the vitreous opacities via a non-invasive approach. By focusing short, intense pulses of laser energy into opaque regions of the transparent vitreous it is possible to raise the temperature of these confined spots to a few 1000° Kelvin. At this temperature, plasma is produced and 'optical breakdown' occurs, with the successful alleviation of floater symptoms in some cases. Typically, Nd:YAG laser is utilised for this purpose (Kwasniewska 2003).

In surgical vitrectomy, the patient’s vitreous and its associated symptomatic vitreous floaters are surgically removed and replaced with balanced salt solution (which is inert and translucent) through small openings in the pars plana. A variety of techniques have been described: conventional 23-gauge pars plana vitrectomy with 3-port trocar (Spandau 2012), bimanual 23-gauge vitrectomy with 4-port trocar (Spandau 2012), 25-gauge pars plana vitrectomy (Sebag 2011), anterior vitrectomy combined with cataract surgery (Mossa 2002), as well as 27-gauge vitrectomy (Oshima 2010).

How the intervention might work

In Nd:YAG laser vitreolysis, a focused pulse of laser energy is used to induce photodisruption of the symptomatic vitreous floaters. When targeted, the irregularities in the vitreous may either undergo disruption locally causing less aberrant transmission of light, or they may become displaced to a region of the vitreous outside the visual axis. Nd:YAG laser vitreolysis has appeared to be most effective if the vitreous floater is central and well defined (Roufail 2006), or well suspended by vitreous strands (Vandorselaer 2001).

As mentioned above, in surgical vitrectomy, the patient’s vitreous and associated symptomatic vitreous floaters are physically removed and replaced with balanced salt solution.

Why it is important to do this review

Symptomatic floaters are a common condition, particularly in the elderly, and can be associated with a significant impact on quality of life.

Increasing age is a strong risk factor for the development of posterior vitreous detachment, or posterior vitreous detachment. Partial or total posterior vitreous detachment has a prevalence of approximately 42% in those aged between 40 and 70 years, 47% between 70 and 75 years, 65% between 75 and 80 years, and 81% in those aged over 80 years old. Optical coherence tomography has identified that partial or complete posterior vitreous detachment had occurred in 80% of elderly patient’s eyes by the day of admission for cataract surgery (Hilford 2009).

People with posterior vitreous detachment are at high risk of experiencing symptomatic floaters. In people who either experience both flashes and floaters or just floaters, posterior vitreous detachment has occurred in 89% and 40% respectively. This highlights the strong association between posterior vitreous detachment and symptomatic floaters (Hikichi 1994).

It has been shown that patients with symptomatic floaters in the absence of other co-morbidities were: (i) willing to shorten their remaining life by 11% to become asymptomatic; and (ii) would undertake a procedure with an 11% mortality rate and 7% risk of blindness if a successful procedure guaranteed elimination of floater symptoms (Wagle 2011). People were willing to make greater sacrifices to cure symptomatic floaters than to cure age-related macular degeneration or glaucoma (Wagle 2011). The impact symptomatic floaters have on quality of life was reported to be as profound as diabetic retinopathy, colon cancer, and asymptomatic human immunodeficiency virus (HIV) infection (Sebag 2011; Wagle 2011).

As posterior vitreous detachment occurs frequently in elderly populations and given 'floaters' are usually the primary symptom associated with posterior vitreous detachment, it is important to establish the most effective means of treating floater symptoms. For patients that require treatment, it is important that both clinicians and patients are able to identify which treatment modality is most effective at treating symptomatic floaters.

In addition, the presence of symptomatic floaters in an eye with an attached vitreous hyaloid may also be caused by the pathological infiltration of cellular or acellular material into the vitreous.

OBJECTIVES

To compare the effectiveness and safety of Nd:YAG laser vitreolysis to pars plana vitrectomy for symptomatic vitreous floaters.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) in this review.

Types of participants

Participants diagnosed with symptomatic vitreous floaters. Conservative management of the symptomatic floaters must have been attempted, without success. There were no restrictions with respect to age, gender, or ethnicity.

Types of interventions

We included trials that compared Nd:YAG laser vitreolysis to pars plana vitrectomy.

Types of outcome measures

Primary outcomes

- Change in vision-related quality of life from baseline to 12 months, as determined by a vision-related quality of life questionnaire. A range of different questionnaires exist (de Boer 2004), and some have demonstrated validity within the domain of people with low vision and have been adapted for use with patients with symptomatic floaters (de Nie 2013; Marella 2010). We did not expect all studies to have utilised the same type of questionnaire.

Secondary outcomes

- Best corrected logMAR or Snellen visual acuity at 12 months for the treated eye(s)
  - If an Early Treatment Diabetic Retinopathy Study (ETDRS) chart was available for a four-metre viewing distance, then it should have been used
- Costs

Adverse outcomes

- The occurrence of sight-threatening complications by 12 months
  - Asymptomatic retinal tears
  - Symptomatic retinal tears
  - Retinal detachment
  - Cataract formation
  - Endophthalmitis

Search methods for identification of studies

Electronic searches

The Cochrane Eyes and Vision Information Specialist conducted systematic searches in the following databases for randomised controlled trials and controlled clinical trials. There were no language or publication year restrictions. The date of the search was 17 January 2017.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 12) (which contains the Cochrane Eyes and Vision Trials Register) in the Cochrane Library (searched 17 January 2017) (Appendix 1);
- MEDLINE Ovid (1946 to 17 January 2017) (Appendix 2);
- Embase Ovid (1980 to 17 January 2017) (Appendix 3);
- LILACS (Latin American and Caribbean Health Science Information database (1982 to 17 January 2017) (Appendix 4);
- ISRCTN registry (www.isrctn.com/editAdvancedSearch; searched 17 January 2017) (Appendix 5);
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 17 January 2017) (Appendix 6);
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched 17 January 2017) (Appendix 7).

Searching other resources

The citations used in this review had their citations analysed for further studies which may have addressed the question of whether Nd:YAG laser vitreolysis or vitrectomy is more effective for treatment of symptomatic floaters. If appropriate, the primary investigators of the applicable trials were contacted to ascertain if they had knowledge of any other relevant trials.

We searched the proceedings of the following conferences from their inception to the current date. If we found suitable abstracts, we planned to contact the authors.

- Research Institute of Ophthalmology international meeting
- Asia-Pacific Academy of Ophthalmology (APAO) Congress
- World Congress on Controversies in Ophthalmology (COPHy)
- European Society of Ophthalmology (SOE)
- Euretina Congress
- Annual Meeting of the American Society of Retina Specialists (ASRS)
- Annual Meeting of the Retina Society
- Meeting of the Club Jules Gonin
- European Association for Vision and Eye Research (EVER)
- European Vitreoretinal Society (EVRS)
- International Vitreoretinal Meeting
- World Ophthalmology Congress
- Pan-American Association of Ophthalmology Congress
- Will's Eye Institute Annual Conference

Data collection and analysis

Selection of studies

Two review authors separately assessed both the titles and abstracts of all articles identified through electronic and manual searches. We only included RCTs as per our predefined inclusion criteria (Types of studies). We obtained the full-text articles of any potentially relevant articles. We planned to enter information from all included studies into the 'Characteristics of included studies' table. For excluded studies, we summarised their characteristics

and reasons for exclusion in the 'Characteristics of excluded studies' table. The two review authors resolved any points of disagreement through discussion, either together or through consultation with a third review author. We illustrated the study selection process in a PRISMA diagram.

Data extraction and management

Two review authors planned to extract data (including outcome data) independently using an electronic form developed by CEV. We intended that one review author would enter data into Review Manager 5 (RevMan 5) (RevMan 2014), and the second review author would review the accuracy of the work performed by the first review author.

Assessment of risk of bias in included studies

Two review authors planned to assess the risk of bias in the included studies using an electronic form developed by CEV. This assessment would include assessing sequence generation, allocation concealment, completeness of data, selective outcome reporting, as well as other potential sources of bias. As an example, allocation concealment helps prevent selection bias, performance bias, detection bias, attrition bias, and reporting bias within studies. We planned to construct a 'Risk of bias' table, which would identify whether any of these types of bias were present in each included study. We also would have included the risk that the bias compromised the results of the study and supporting evidence for these judgments. Two review authors would conduct these assessments and we planned to resolve any disagreements by consensus or arbitration by a third review author.

Measures of treatment effect

Our measure of effect for dichotomous outcomes (complications) would have been the risk ratio (RR). Our measure of effect for continuous outcomes (vision-related quality of life, visual acuity) would have been the mean difference (MD).

Unit of analysis issues

In our analysis, we planned to compare eyes treated with Nd:YAG laser vitreolysis with those treated with pars plana vitrectomy. People may experience symptomatic floaters from one eye or both eyes, and one eye may be more symptomatic than the other. Included studies would have randomised participants to one or the other treatment modality, and may have either treated one or both eyes using this assigned treatment modality. We planned to record details of the study design with respect to treatment modality and treatment of either one or both eyes. If insufficient information was available in the trial report, we planned to contact the study authors for clarification. For our outcome measures, changes to the participant's quality of life would have been measured at the 'participant level' using the questionnaire, visual acuity would have been measured in treated eye(s), and costs would have been divided by the number of treated eyes. We planned to document the study design with respect to unit of analysis issues for each study and planned to approach the study authors for clarification if necessary.

Dealing with missing data

We anticipated that missing data would have been present within the included studies. We planned to analyse studies using an available case analysis. We planned to collect the percentages of missing data from each intervention group in all studies, and examine the reasons for loss to determine whether it meets the assumption of data being missing at random. We planned to consider studies exhibiting unequal rates (greater than 20%) of missing data between intervention groups to be at risk of attrition bias.

Assessment of heterogeneity

We planned to assess heterogeneity of treatment effects across studies using the Chi^2 test, and we planned to use the I^2 statistic to identify the percentage of the variability in effect estimates that was due to heterogeneity rather than sampling error (chance) (Higgins 2002). We planned to generate forest plots and assess them for direction and size of the effect. We would not have reported pooled data either when heterogeneity is found to be significant (Chi^2 test P value of less than 0.10, or when the I^2 statistic value was greater than 50%).

Assessment of reporting biases

We planned to assess publication bias by means of the adjusted rank correlation test (Begg's test) and the regression-based test (Egger's test) (Begg 1994; Egger 1997). Graphically, we planned to assess the extent of publication bias using a funnel plot with pseudo 95% confidence intervals (CIs). We would have needed to have included at least 10 trials in this meta-analysis in order to consider this type of analysis appropriate.

Data synthesis

We planned to perform meta-analyses either using the random-effects model or the fixed-effect model based on our assessment of between-study heterogeneity. However, we expected included studies to be heterogenous based on our prior knowledge of this topic. We planned to perform random-effects meta-analyses to analyse MDs in the outcomes of ordinal data (e.g. quality of life scales) between the two groups (vitreolysis versus pars plana vitrectomy), and in additional effect estimates (e.g. RRs) between the two groups.

Subgroup analysis and investigation of heterogeneity

We anticipated performing three subgroup analyses: firstly, we would have compared the treatment effects in people with high myopia (−6 dioptres or greater) compared to people without high myopia (less than −6 dioptres), secondly we would have compared the treatment effects in people aged 65 and older compared to people younger than 65, and thirdly we would have compared males with females.

Depending on the number of trials, we may have performed meta-regression to investigate the effect size of the following characteristics.

- Presence of any ocular co-morbidities including previous cataract surgery prior to enrolment in the trial
- Visual acuity at enrolment in the trial
- If the energy and total number of Nd:YAG laser shots applied during vitreolysis varies between studies
- Follow-up questionnaire at other time-points, such as after 6, 18, or 24 months after the initial procedure
- Questionnaire responses for patients who suffered complications from treatment

Sensitivity analysis

We planned to perform sensitivity analyses to assess robustness of pooled estimates. We planned to exclude studies that were at high risk of bias in one or more 'Risk of bias' domains.

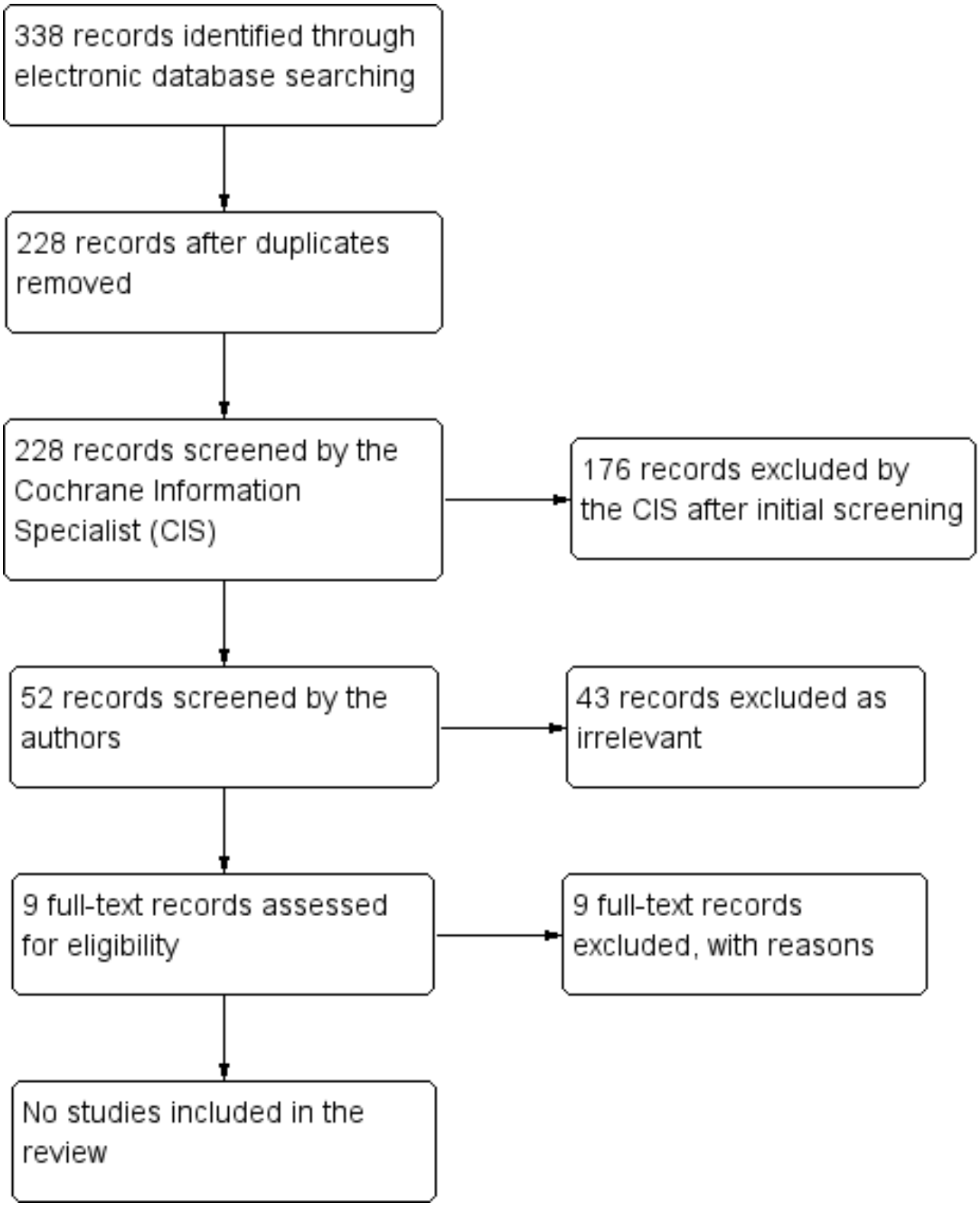
RESULTS

Description of studies

Results of the search

The electronic searches yielded 338 references (Figure 1). After removal of 100 duplicates, the Cochrane Information Specialist (CIS) screened the remaining 228 records and removed 176 references which were irrelevant to this review. We screened the remaining 52 references and obtained the full-text reports of nine references for further assessment. We did not find any randomised controlled trial (RCT) or quasi-RCT that met the inclusion criteria of this review.

Figure 1. Study flow diagram.



Included studies

We did not identify any studies that were eligible for inclusion in this review.

Excluded studies

We did not identify any studies that were relevant to the objectives of this systematic review. Our reasons for exclusion of studies included the following.

- Studies were not RCTs
- RCTs had not yet begun recruiting participants
- RCTs had allocated participants into either none or only one of the two types of intervention being examined in this review
  * For instance, we excluded studies if they only assigned participants into Nd:YAG laser vitreolysis and "sham laser" treatment arms, rather than Nd:YAG laser vitreolysis and vitrectomy treatment arms
  * We listed any ongoing or completed RCTs that randomised participants to one of the two required treatment arms and a 'sham treatment' in the 'Characteristics of excluded studies' tables

Risk of bias in included studies

We did not find any trials that were eligible for inclusion in the review for assessment of risk of bias.

Effects of interventions

We found no information on the effects of interventions as no trials met the inclusion criteria of this review.

DISCUSSION

The literature currently published on this subject is limited to retrospective case reports and retrospective cohort studies (de Nie 2013). We only planned to include randomised controlled trials (RCTs) that met the eligibility criteria specified in the protocol (Kokavec 2015), but as there is also no validated technique to exhaustively retrieve and assess observational studies, this review is likely to have not assessed all the data present within the literature. As RCTs offer the ability to make causal inferences, these studies provide the strongest evidence for a treatment's effectiveness. Furthermore, RCTs are designed to minimise bias and confounding of unknown variables (Levin 2007). It would therefore be misleading to draw conclusions from studies other than RCTs. Appropriate RCTs need to be undertaken to empower clinicians to use strong evidence during consultations with patients on the risks and benefits of undertaking a vitrectomy or Nd:YAG laser vitreolysis for troublesome floater symptoms. This Cochrane Review sought to primarily answer the clinical question of which of two interventions, Nd:YAG laser vitreolysis or pars plana vitrectomy, were most effective at treating symptomatic floaters. We did not seek to identify whether either one of these two interventions was superior to sham treatment.

Summary of main results

There are currently no RCTs that directly compare the effectiveness of Nd:YAG laser vitreolysis to pars plana vitrectomy for the treatment of symptomatic floaters.

Overall completeness and applicability of evidence

We believe that our conclusions are supported by a thorough search of available evidence, as outlined in the published protocol (Kokavec 2015).

Quality of the evidence

We did not identify any trials for inclusion in this review.

Potential biases in the review process

We may be unaware of individuals or organisations who have conducted or may be conducting relevant RCTs. Therefore it is possible we did not identify relevant RCTs. We identified ongoing and completed RCTs that assigned participants to receive only one of the two treatment modalities required for inclusion in this review (NCT01970267; NCT02812004; NCT02897583. We did not identify any ongoing or completed RCTs that assigned participants to both Nd:YAG laser vitreolysis and pars plana vitrectomy treatment arms.

Agreements and disagreements with other studies or reviews

We are unaware of any other studies or reviews that have directly compared Nd:YAG laser vitreolysis against vitrectomy for the treatment of symptomatic floaters.

AUTHORS' CONCLUSIONS

Implications for practice

As we did not identify any randomised clinical trials that compared the effectiveness of Nd:YAG laser vitreolysis to vitrectomy for symptomatic floaters, ophthalmologists do not have strong evidence to recommend vitrectomy over Nd:YAG laser vitreolysis (or visa versa) for the treatment of symptomatic floaters. Whilst there are specific ongoing and completed clinical trials that compare Nd:YAG laser vitreolysis to 'sham' Nd:YAG laser vitreolysis for symptomatic floaters (NCT01970267; NCT02812004; NCT02897583, these studies were not designed to assess how Nd:YAG laser vitreolysis compares to vitrectomy for the treatment of symptomatic floaters.

Implications for research

Properly designed RCTs are needed to evaluate the treatment outcomes from the interventions described. We recommend future studies randomise participants to either a Nd:YAG laser vitreolysis group or a vitrectomy group, with participants in each group assigned to either receive treatment or a sham intervention. Care must be taken to preserve allocation concealment and minimise other sources of bias. Treatment within the Nd:YAG laser vitreolysis group should present relevant treatment properties, such as the laser pulse duration, laser power intensity, total number of number of laser shots fired, and the anatomical location of the laser shots of where the laser shots were fired (in relation to the distance from the eye's visual axis, posterior lens capsule, and neuroretina).

Future studies should follow participants at six months and 12 months after the intervention. Also they should use best corrected visual acuity (BCVA) using an Early Treatment of Diabetic Retinopathy Study (ETDRS) chart read at 4 metres, vision-related quality of life (VRQOL), and adverse outcomes as the outcome measures of the trial.

Each of these outcome measures require a threshold of change from baseline which signifies an improvement. This threshold is frequently referred to as the minimal clinically important difference (MCID). We suggest the MCID for visual acuity be set at an improvement of 2 lines on an Early Treatment of Diabetic Retinopathy Study (ETDRS) chart read at 4 metres, in line with other ophthalmic studies (Jackson 2017).

Following vitrectomy of symptomatic floaters, one study has shown a weak but significant correlation between postoperative BCVA and patient satisfaction on a VRQOL questionnaire (a modified version of the NEI VFQ-25 questionnaire) (Pearson correlation coefficient of 0.41; P < 0.0001). Furthermore, the authors also revealed a significant (albeit even weaker) correlation between change of BCVA (from pre-operatively to post-operatively) and scores in this questionnaire (Pearson correlation coefficient: 0.28; P = 0.004) (de Nie 2013).

At the time of writing there is no accepted or reported MCID threshold for scores on VRQOL questionnaires for participants with symptomatic floaters. Owing to the apparently weak correlation between BCVA and scores on VRQOL questionnaires, we suggest that the MCID for VRQOL questionnaires represent a score improvement exceeding one standard error of the mean (1 SEM) on these questionnaires. This SEM method is a valid approach to MCID determination (Guyatt 2002; Wyrwich 1999) which has been utilised by other ophthalmic studies (Jackson 2017; Naik 2013).

There will be ethical factors to consider during participant selection for future clinical trials. For instance, most ophthalmologists will be averse to attempting Nd:YAG laser vitreolysis on a vitreous floater suspended close to a region of healthy retinal tissue or the posterior lens capsule for the risk of inducing a laser burn to unintended tissue.

The rate of cataract formation may be high in one or both treatment arms. To explore the differential risk of visual disablement arising from treatment-related cataracts within the vitrectomy or Nd:YAG vitreolysis treatment arms, authors are encouraged to ask all study participants to complete an appropriate cataract-specific questionnaire at 12 months after treatment. In subsequent versions of this meta-analysis, the questionnaire scores from each treatment arm may be evaluated to determine if either treatment arm has a significantly higher rate of cataract formation. Cataract formation by 12 months after treatment is considered a sight-threatening adverse outcome in this meta-analysis.

Finally, as recent studies suggest floaters may reduce contrast sensitivity (Sebag 2014), contrast sensitivity may therefore affect patient responses on VRQOL questionnaires (Mamou 2015). As such, authors would be well advised to evaluate the contrast sensitivity of participants at each specified follow-up visit.

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REFERENCES

References to studies excluded from this review

de Nie 2013 *{published data only}*

de Nie KF, Crama N, Tilanus MA, Klevering BJ, Boon CJ. Pars plana vitrectomy for disturbing primary vitreous floaters: clinical outcome and patient satisfaction. *Graefe's Archive for Clinical and Experimental Ophthalmology* 2013;**251**(5):1373-82.

Martínez-Sanz 2009 *{published data only}*

Martínez-Sanz F, Velarde JI, Casuso P, Fernández-Cotero JN. Surgical solution to vitreous floaters visual problem [Solucion quirurgica al problema visual de los cuerpos vitreos flotantes]. *Archivos de la Sociedad Espanola de Oftalmologia* 2009;**84**(5):259-62.

NCT01970267 *{published data only}*

NCT01970267. Randomized trial of laser ablation for highly symptomatic floaters. clinicaltrials.gov/ct2/show/NCT01970267 (first received 22 October 2013).

NCT02812004 *{published data only}*

NCT02812004. New horizons in the treatment of vitreous floaters (Ellex) [New horizons in the treatment of vitreous floaters: efficacy and safety of vitreolysis with the Ultra Q Reflex YAG laser (Ellex)]. clinicaltrials.gov/ct2/show/NCT02812004 (first received 17 June 2016).

NCT02897583 *{published data only}*

NCT02897583. YAG vitreolysis for floaters [A prospective randomized controlled trial evaluating the safety and efficacy of YAG vitreolysis versus sham for symptomatic Weiss ring due to posterior vitreous detachment]. clinicaltrials.gov/ct2/show/NCT02897583 (first received 16 June 2016).

Ruiz-Moreno 1998 *{published data only}*

Ruiz-Moreno J. Retinal detachment after vitreolysis with the Nd: YAG laser. *Lasers and Light in Ophthalomology* 1998;**8**:231-4.

Schulz-Key 2011 *{published data only}*

Schulz-Key S, Carlsson JO, Crafoord S. Longterm follow-up of pars plana vitrectomy for vitreous floaters: complications, outcomes and patient satisfaction. *Acta Ophthalmologica* 2011;**89**(2):159-65.

Sebag 2014 *{published data only}*

Sebag J, Yee KM, Wa CA, Huang LC, Sadun AA. Vitrectomy for floaters: prospective efficacy analyses and retrospective safety profile. *Retina* 2014;**34**(6):1062-8.

Toczołowski 1998 *{published data only}*

Toczołowski J, Katski W. Use of Nd:YAG laser in treatment of vitreous floaters. *Klinika Oczna* 1998;**100**(3):155-7.

Additional references

Begg 1994

Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;**50**(4):1088-101.

Bishop 2000

Bishop PN. Structural macromolecules and supramolecular organisation of the vitreous gel. *Progress in Retinal and Eye Research* 2000;**19**(3):323-44.

de Boer 2004

de Boer MR, Moll AC, de Vet HC, Terwee CB, Völker-Dieben HJ, van Rens GH. Psychometric properties of vision-related quality of life questionnaires: a systematic review. *Ophthalmic and Physiological Optics* 2004;**24**(4):257-73.

Egger 1997

Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629-34.

Glanville 2006

Glanville JM, Lefebvre C, Miles JN, Camosso-Stefinovic J. How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association* 2006;**94**(2):130-6.

Guyatt 2002

Guyatt GH, Osoba D, Wu AW, Wyrwich KW, Norman GR. Methods to explain the clinical significance of health status measures. *Mayo Clinic Proceedings* 2002;**77**(4):371-83.

Higgins 2002

Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;**21**(11):1539-58.

Hikichi 1994

Hikichi T, Trempe CL. Relationship between floaters, light flashes, or both, and complications of posterior vitreous detachment. *American Journal of Ophthalmology* 1994;**117**(5):593-8.

Hilford 2009

Hilford D, Hilford M, Mathew A, Polkinghorne PJ. Posterior vitreous detachment following cataract surgery. *Eye* 2009;**23**(6):1388-92.

Jackson 2017

Jackson TL, Verstraeten T, Duchateau L, Lescrauwaet B. Visual function response to ocriplasmin for the treatment of vitreomacular traction and macular hole. *Acta Ophthalmologica* 2017 Jan 30 [Epub ahead of print]. [DOI: 10.1111/aos.13369]

Kwasniewska 2003

Kwasniewska S. Some applications of the neodymium:YAG laser operating in the thermal and photodisruptive modes. Vitreolysis. In: Fankhauser F, Kwasniewska S editor(s). Lasers in Ophthalmology: Basic, Diagnostic, and Surgical Aspects: a Review. Amsterdam: Kugler Publications, 2003:403-13.

Levin 2007

Levin KA. Study design VII. Randomised controlled trials. *Evidence-Based Dentistry* 2007;**8**(1):22–3.

Mamou 2015

Mamou J, Wa CA, Yee KM, Silverman RH, Ketterling JA, Sadun AA, et al. Ultrasound-based quantification of vitreous floaters correlates with contrast sensitivity and quality of life. *Investigative Ophthalmology & Visual Science* 2015;**56**(3):1611-7.

Marella 2010

Marella M, Pesudovs K, Keeffe JE, O'Connor PM, Rees G, Lamoureux EL. The psychometric validity of the NEI VFQ-25 for use in a low-vision population. *Investigative Ophthalmology & Visual Science* 2010;**51**(6):2878-84.

Mossa 2002

Mossa F, Delaney YM, Rosen PH, Rahman R. Floaterectomy: combined phacoemulsification and deep anterior vitrectomy. *Journal of Cataract and Refractive Surgery* 2002;**28**(4):589-92.

Naik 2013

Naik RK, Gries KS, Rentz AM, Kowalski JW, Revicki DA. Psychometric evaluation of the National Eye Institute Visual Function Questionnaire and Visual Function Questionnaire Utility Index in patients with non-infectious intermediate and posterior uveitis. *Quality of Life Research* 2013;**22**(10):2801-8.

Oshima 2010

Oshima Y, Wakabayashi T, Sato T, Ohji M, Tano Y. A 27-gauge instrument system for transconjunctival sutureless microincision vitrectomy surgery. *Ophthalmology* 2010;**117**(1):93-102.e2.

RevMan 2014 [Computer program]

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Roufail 2006

Roufail ED, Polkinghorne P. Vitreous floaters. *Comprehensive Ophthalmology Update* 2006;**7**(4):171-7.

Sebag 2009

Sebag J. Vitreous: the resplendent enigma. *British Journal of Ophthalmology* 2009;**93**(8):989-91.

Sebag 2011

Sebag J. Floaters and the quality of life. *American Journal of Ophthalmology* 2011;**152**(1):3-4.e1.

Sendrowski 2010

Sendrowski DP, Bronstein MA. Current treatment for vitreous floaters. *Optometry* 2010;**81**(3):157-61.

Spandau 2012

Spandau U, Heimann H. Practical Handbook for Small-Gauge Vitrectomy: A Step-By-Step Introduction to Surgical Techniques. Berlin-Heidelberg: Springer-Verlag, 2012.

Vandorselaer 2001

Vandorselaer T, Van De Velde F, Tassignon MJ. Eligibility criteria for Nd-YAG laser treatment of highly symptomatic vitreous floaters. *Bulletin de la Societe Belge d'Ophtalmologie* 2001;**280**:15-9.

Wagle 2011

Wagle AM, Lim WY, Yap TP, Neelam K, Au Eong KG. Utility values associated with vitreous floaters. *American Journal of Ophthalmology* 2011;**152**(1):60-5.e1.

Wyrwich 1999

Wyrwich KW, Tierney WM, Wolinsky FD. Further evidence supporting an SEM-based criterion for identifying meaningful intra-individual changes in health-related quality of life. *Journal of Clinical Epidemiology* 1999;**52**(9):861-73.

Yanoff 2008

Yanoff M, Duker JS. Ophthalmology. 3rd Edition. St Louis: Mosby Elsevier, 2008.

References to other published versions of this review

Kokavec 2015

Kokavec J, Wu Z, Sherwin JC, Ang AJS, Ang G. Laser or vitrectomy for vitreous floaters. *Cochrane Database of Systematic Reviews* 2015, Issue 4. [DOI: 10.1002/14651858.CD011676]

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
de Nie 2013	This study is not a RCT
Martínez-Sanz 2009	This study is not a RCT
NCT01970267	This randomised controlled trial (RCT) only assigned participants into a) laser vitreolysis or b) "sham" laser vitreolysis treatment arms
NCT02812004	This RCT only assigned participants to a) laser vitreolysis or b) "sham" laser vitreolysis treatment arms

Study	Reason for exclusion
NCT02897583	This RCT only assigned participants to a) laser vitreolysis or b) "sham" laser vitreolysis treatment arms
Ruiz-Moreno 1998	This study is not a RCT
Schulz-Key 2011	This study is not a RCT
Sebag 2014	This study is not a RCT
Toczołowski 1998	This study is not a RCT

Abbreviations: RCT: randomised controlled trial.

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Vitreous Body] this term only
#2 vitreous near/2 (degenerat* or floater*)
#3 vitreous near/2 (body or bodies or humor*)
#4 floaters
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Laser Therapy] this term only
#7 MeSH descriptor: [Lasers, Solid-State] this term only
#8 vitreolysis
#9 YAG
#10 #6 or #7 or #8 or #9
#11 MeSH descriptor: [Vitrectomy] this term only
#12 PPV*
#13 vitrectom*
#14 #11 or #12 or #13
#15 #5 and #10 and #14

Appendix 2. MEDLINE Ovid search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. Vitreous Body/
14. (vitreous adj2 (degenerat$ or floater$)).tw.
15. (vitreous adj2 (body or bodies or humor$)).tw.
16. floaters.tw.
17. or/13-16
18. Laser Therapy/
19. Lasers, Solid-State/
20. vitreolysis.tw.
21. YAG.tw.
22. or/18-21

23. vitrectomy/
24. PPV$.tw.
25. vitrectom$.tw.
26. or/23-25
27. 17 and 22 and 26
28. 12 and 27

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville 2006.

Appendix 3. Embase Ovid search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin$ adj3 trial$).tw.
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. Vitreous Floaters/
34. Vitreous Body/
35. Vitreous Opacity/
36. (vitreous adj2 (degenerat$ or floater$)).tw.
37. (vitreous adj2 (body or bodies or humor$)).tw.
38. floaters.tw.
39. or/34-37
40. Laser Surgery/
41. Neodymium Yag Laser/
42. vitreolysis.tw.
43. YAG.tw.
44. or/40-43
45. vitrectomy/
46. PPV$.tw.
47. vitrectom$.tw.
48. or/45-47
49. 39 and 44 and 48
50. 32 and 49

Appendix 4. LILACS search strategy

Vitreous degeneration OR floaters and Laser OR YAG OR Vitrectomy OR PPV

Appendix 5. ISRCTN search strategy

(vitreous degeneration) OR floaters

Appendix 6. ClinicalTrials.gov search strategy

(Vitreous Degeneration OR Floaters) AND (Laser OR YAG) AND (Vitrectomy OR PPV)

Appendix 7. WHO ICTRP search strategy

(Vitreous Degeneration OR Floaters) = Condition AND (Laser OR YAG OR Vitrectomy OR PPV) = Intervention

CONTRIBUTIONS OF AUTHORS

JK conceived the review.
JCS, ZW, and AJA provided general advice on the review.
JK, JCS, ZW, AJA, and GSA designed the review.
JK and GSA co-ordinated the review.

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JK: none known.
ZW: none known.
JCS: none known.
AKSA: none known.
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INDEX TERMS

Medical Subject Headings (MeSH)

Eye Diseases [*surgery]; Lasers, Solid-State [*therapeutic use]; Vitrectomy [*methods]

MeSH check words

Humans